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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,562	03/06/2007	Tony George	Y0087.70013US01	4715

23628 7590 03/18/2009

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
03/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,562	GEORGE ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 25-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 25-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/20/06, 1/07/09, 2/19/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-8 and 25-36 are currently pending in the application.

Applicant's election of Group I (i.e. a method of treating a mood disorder) and election of mecamylamine as the nACH receptor antagonist and citalopram as the additional agent in the reply filed on 01/07/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is deemed proper and is therefore made FINAL.

IDS

The information disclosure statements (IDS) submitted on 11/20/06, 01/07/09, and 02/19/09 are acknowledged and have been entered. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Popik et al. (British Journal of Pharmacology, 2003, Vol. 139, pgs. 1196-1202, cited by applicant and filed on an IDS 1449) in view of Shytle et al. (U.S. 6,734,215 B2, cited by applicant and filed on an IDS 1449).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Popik et al. teach that epidemiological and clinical observations suggest the involvement of nicotinic acetylcholine receptors (nAchRs) in depressive illness (see abstract, section 1). In fact, lines of evidence indicate that nAChRs are involved in major depression (a.k.a. major depressive disorder; instant claim 2; see pg. 1196, left col., Introduction, paragraph 2 and right col., paragraph 2). Thus, Popik et al. sought to determine if nAChRs antagonists produce antidepressant like effects (i.e. AD; see pg. 1197, left col., paragraph 3). In his study, Popik et al. investigated if the nAChR antagonist, mecamylamine or MEC, produced and/or influenced AD-like effects of citalopram (instant claims 3-7; see pg. 1197, left col., last paragraph). Particularly, Popik et al. demonstrated that co-treatment of 2 mg/kg of body weight of citalopram (i.e. CIT) and 2.5 mg of mecamylamine (i.e. MEC) significantly inhibited the immobility in the tail-suspension test (see pg. 1199, left col., paragraph 2 and abstract) suggesting a positive effect on the depression. Importantly, Popik et al. demonstrated that the interaction between nAChR antagonists and CIT appeared to produce a synergistic effect (see abstract and pg. 1200, right col., last paragraph).

Popik et al. do not specifically teach a method of treating refractory major depression in an individual suffering from mood disorder or the use of MEC and CIT as a single formulation.

While Popik et al. teach sequential administration of MEC and CIT to mice, Popik et al. also indicated that the tail-suspension test is typically used to test anti-depressant

effects (see pg. 1197, last paragraph). Moreover, it would be well within the purview of the skilled artisan to formulate MEC in the same formulation as CIT since Popik et al. demonstrated that both MEC and CIT act in a synergistic manner.

Fava is being provided to demonstrate that unipolar depressive disorders (i.e. major depression or major depressive disorder) entails treatment resistant depression (i.e. refractory major depression) and is characterized by the occurrence of an inadequate response following adequate antidepressant therapy among such patients and consequently such patients fail to achieve remission (see pg. 649, left col., Introduction and abstract). Fava further teach that such depression also include the types of depression that are non-responsive as well wherein the goal for such depression should be complete remission (see pg. 649, left col., Introduction and abstract).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Popik et al. to refractory patients of major depression since Fava teaches that major depression entails resistant major depression patients who are non-responsive to adequate antidepressant therapy. Moreover, one of ordinary skill in the art would have found it obvious to formulate both mecamylamine and citalopram as a single formulation since it would be well within the purview of the skilled artisan to formulate the compounds as a single formulation and given their synergistic effects. Thus, given the teachings of Popik and Fava, one of ordinary skill

would have been motivated to mecamylamine and citalopram as a single formulation and administer the formulation to refractory major depressive disorder patients with the reasonable expectation of providing a method that is effective in treating such subset of major depressive disorder patients.

Claims 1-8 and 25-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Popik et al. (British Journal of Pharmacology, 2003, Vol. 139, pgs. 1196-1202, cited by applicant and filed on an IDS 1449) in view of Shytle et al. (U.S. 6,734,215 B2, cited by applicant and filed on an IDS 1449) as applied to claims 1-8 above and in further view of Shytle et al. (U.S. 6,734,215 B2).

The Popik and Fava references are as discussed above and incorporated by reference herein. However, Popik and Fava do not teach administration of exo-S-mecamylamine that is substantially free of exo-R-mecamylamine.

Shytle et al. teach the use of exo-S-mecamylamine or a pharmaceutically acceptable carrier salt thereof, substantially free of its exo-R-mecamylamine, said amount being sufficient to ameliorate neuropsychiatric disorders including depression (instant claims 25 and 36; see abstract, col. 5, lines 16-22, and col. 9, lines 29-38). Shytle et al. further teach that the aforementioned formulation for improved therapy with fewer side effects and for improved medical compliance, quality of life and social functioning (see col. 5, lines 25-32). Particularly, Shytle et al. teach that the pharmaceutical composition include a therapeutically effective of exo-S-mecamylamine

or its pharmaceutically acceptable salt with a carrier in an amount of about 0.5 mg to about 1000 mg (instant claim 31; see col. 5, lines 33-67 and col. 6, lines 1-11). Shytle et al. further teach that the formulation can be administered one to four times per day (instant claim 32; see col. 24, claims 7-11).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the exo-S-mecamylamine of Shytle et al. into the method of Popik et al. and administer the combination of exo-S-MEC with CIT to refractory patients with major depressive disorder since Fava teaches that major depression or major depressive disorder entails resistant-major depression patients who are non-responsive to adequate antidepressant therapy and given that Shytle et al. teach that the exo-S-MEC possess fewer side effects and help in achieving patient compliance. Moreover, one of ordinary skill in the art would have found it obvious to formulate both mecamylamine and citalopram as a single formulation since it would be well within the purview of the skilled artisan to formulate the compounds as a single formulation given their synergistic effects. Thus, given the teachings of Shytle, Popik, and Fava, one of ordinary skill would have been motivated to substitute exo-S- mecamylamine for the mecamylamine of Popik et al. and further combined it with citalopram as a single formulation and administer the formulation to refractory major depressive disorder patients with the reasonable expectation of providing a method with fewer side effects that is effective in treating such subset of major depressive disorder patients and a method that helps in improving patient compliance.

Popik et al. do not disclose the exact dosage of Citalopram (CIT) as applicant. However, Popik et al. do teach CIT at a dosage of 2mg/kg of body weight. Consequently, it is well within the purview of the skill of the artisan at the time of the invention to adjust the dosage of CIT depending on the patient to be treated during the course of routine experimentation so as to obtain the most effective CIT dosage.

While the exact dosage of CIT is not disclosed by Popik et al., it is generally noted that differences in dosages do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges or dosages of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of ranges is the optimum combination of dosages.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

03/14/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617